

REMARKS

This is in response to the Office Action dated April 14, 2010. The due date for response has been extended one month from July 14, 2010, to August 14, 2010, by paying appropriate government fees. Claims 1-9 are pending. Claims 2 and 6 are amended herewith to correct typographical errors which occurred subsequent to the initial filing of the claims. No claim is herewith added or deleted. Thus, with the entry of this response, claims 1-9 will remain active. No new matter is added with the amendment.

I. Miscellaneous

Applicants thank Examiner Pihonak for withdrawing the previous rejections under 35 USC §§ 112 and 102(b).

II. Rejections under 35 USC § 103

The Examiner rejects claims 1-9 under 35 USC § 103 as being unpatentable over Suh (WO 03/007947), hereinafter "Suh", in view of Karsenty et al. (WO 01/53477) hereinafter "Karsenty", and further in view of Allen et al. (US Patent No. 5,914,329), hereinafter "Allen". The Examiner admits that Suh does not teach dimethanesulfonic acid salts of N-hydroxy-4- {5- [4-(5-isopropyl-2-methyl-1,3 -thiazol-4-yl)phenoxy]pentoxy}benzamide. Kartesenty is cited for allegedly teaching that a variety of different neuropeptide Y receptor antagonists can be used for treating conditions related to decreased bone mass and that salts of such antagonists may be dimesylate salts, which the Examiner explains are the ionic form of di-methanesulfonic acid. Allen is cited for allegedly teaching that neuropeptide Y ligands are used to treat a variety of disorders associated with excess neuropeptide Y and that the dimesylate salt of the active agent is preferred as it has good solubility, stability, good bioavailability and is non-hydroscopic in increased humidity, in comparison to other salts. Allen also is cited for allegedly teaching various excipients, such as calcium carbonate and calcium phosphate. The Examiner concludes that one of ordinary skill in the art at the time of the invention, would have been motivated to prepare the dimesylate (or di-methanesulfonic acid salt) of N-hydroxy-4- {5-

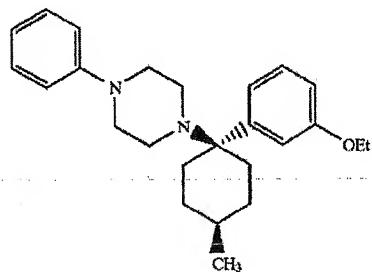
[4-(5-isopropyl-2-methyl-1,3 -thiazol-4-yl)phenoxy]pentoxy}benzamide, because Suh teaches that the methanesulfonic acid salt is the preferred salt of this compound, which is effective for treating osteoporosis and Karsenty and Allen teach that dimesylate salt of active agents used to treat osteoporosis have better solubility, stability and bioavailability in comparison to other pharmaceutically acceptable salts. This combination, according to the Examiner, would have provided an expectation of success in preparing the compound of the invention with improved solubility, stability and bioavailability. Applicants respectfully but vigorously traverse this rejection.

The present invention is in the chemical/pharmaceutical arts. Courts have considered the chemical and pharmaceutical arts to be “unpredictable.” Because chemistry and pharmaceuticals are unpredictable arts, courts also have concluded that the identification of solutions in these arts would be less obvious. *Esai Co., Ltd v. Dr. Reddy's Laboratories Ltd.*, 533 F. 3d 1353 (Fed. Cir. 2008).

Typically, an obviousness analysis in the chemical arts asks why one of skill in the art would have selected a lead compound that is structurally similar to the compound in question and then asks why one would have been motivated to modify that compound. *Takeda Chem. Indus. Ltd. v. Alphapharm Pty Ltd.*, 492 F.3d 1350, 1359-60 (Fed Cir. 2007) A small structural modification in a chemical compound can have unpredictable consequences. Here, the Examiner cites Suh for disclosing a lead compound and then cites two secondary references, Karsenty and Allen, to support an alleged motivation toward, and expectation of success in, modifying that compound. However, the two secondary references describe chemical compounds that have nothing structurally in common with the compound of the present invention. Rather, they simply share a use with the claimed compound. Applicants assert that despite their disclosure of compounds that may treat bone disease, Karsenty and Allen are not relevant to the claimed compound and accordingly would not have motivated the skilled artisan to produce N-hydroxy-4- {5- [4-(5-isopropyl-2-methyl-1,3 -thiazol-4-yl)phenoxy]pentoxy}benzamide 2 methanesulfonic acid salt.

Methanesulfonic acid salts of other compounds already existed at the time of the invention. But, each chemical compound has its own specific chemical structure, and various salts may exist according to this structure. The particular qualities of a salt may vary depending on the general structure of the compound upon which the salt is based. That is, whether a specific salt has improved solubility is determined by its specific chemical structure. Accordingly, certain specific salts of different compounds have improved solubility, whereas others do not. Results are unpredictable. Whether a specific salt of a compound has improved solubility can only be determined through experimentation.

Karsenty (WO 01/53477) and Allen (US Patent No. 5914329) describe cis-1-(3-ethoxyphenyl)-1-(4-phenylpiperazin-1-yl)-4-methyl-cyclohexane, as follows:



As stated above, this compound is completely different from the compound N-hydroxy-4- {5- [4-(5-isopropyl-2-methyl-1,3-thiazol-4-yl)phenoxy]pentoxy}benzamide of the present invention and the improved results reported in Karsenty and Allen would have no bearing on a different compound. Karsenty and Allen do not suggest otherwise. One of skill in the art of the invention would have known that the functionality of a given salt of a compound is unique to that compound. The fact that two structurally dissimilar compounds may be used to treat similar diseases does not change this. Therefore, the dimesylate of 'cis-1-(3-ethoxyphenyl)-1-(4-phenylpiperazin-1-yl)-4-methyl-cyclohexane' would not have led the skilled artisan to the 2 methanesulfonic acid of N-hydroxy-4-{5- [4-(5-isopropyl-2-methyl-1,3-thiazol-4-yl)phenoxy]pentoxy}benzamide. .

As for the Examiner's reliance upon Suh's teachings, applicants again argue that such teachings are general and do not direct the skilled artisan to 2

methanesulfonic acid. Although applicants vigorously disagree that the claimed compound would have been *prima facie* obvious in view of Suh and the secondary references, applicants also disagree with the Examiner's reluctance to accept their evidence of unexpected and surprising properties that would rebut a finding of *prima facie* obviousness (*In Re Dillon*, 919 F.2d 688, 696 (Fed. Cir. 1990)). That is, applicants show in Examples 2 and 4 of the application that 2 methanesulfonic acid salt of DW1350 has an effect that is superior over the 1 methanesulfonic acid salt of DW1350 and is also superior over the free base of DW1350. In particular, in examining solubility (Table 3) and pharmacokinetic properties (Table 5), it is clearly shown that the 2 methanesulfonic acid salt of DW1350 is superior over the free base of DW1350 and is superior over the 1 methanesulfonic acid salt of DW1350. In light of these data, and the unpredictability of the art of the invention, the claimed compound is non-obvious over the prior art. Withdrawal of this rejection is therefore respectfully requested.

III. Double Patenting Rejections

The Examiner has provisionally rejected claims 1 and 3-9 for obviousness type double patenting over claims 1-8, 10-11 and 13 of copending application no. 11/577,469. Applicants respectfully traverse this rejection. In further response, applicants submit herewith a Terminal Disclaimer to render this objection moot.

The Examiner has rejected claims 1-9 for obviousness type double patenting over claims 1-3, 5-8, 9-11, and 13-15 of U.S. Patent No. 7,662,840 (this corresponds to "Suh"). Applicants respectfully traverse this rejection for reasons set forth above in connection with the obviousness rejection over Suh. Claims 1-3, 5-8, 9-11, and 13-15 of U.S. Patent No. 7,662,840 recite salts generally or recite methane sulfonate (claim 8) and do not guide the skilled artisan towards 2 methansulfonic acid. Because the art of the invention is unpredictable and U.S. Patent No. 7,662,840 does not direct one of skill in the art to 2 methanesulfonic acid of N-hydroxy-4-{5- [4-5-isopropyl-2-methyl-1,3-

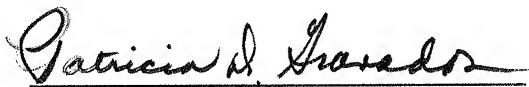
thiazol-4-yl)phenoxy]pentoxy}benzamide, this rejection is improper and withdrawal thereof is respectfully requested.

CONCLUSION

In view of the above arguments and the attached Terminal Disclaimer, applicants respectfully request the Examiner to reconsider and withdraw all outstanding rejections. A Notice of Allowance is respectfully requested. The Examiner is invited to contact the undersigned attorney for applicant for any reason related to the advancement of this case.

In the event that additional fees are necessary in view of this amendment or the Examiner's Amendment, then such fees are hereby authorized to be charged to our Deposit Account No. 01-2300 referencing docket number 027707.00031.

Respectfully submitted,



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